UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,343	04/11/2005	Jacques Mallet	3665-122	3751

23117 7590 11/14/2006

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/511,343	MALLET ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 17, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,36 and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,36 and 47-67* is/are rejected.

7)☒ Claim(s) *43-46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response of August 17, 2006, to the non-final action dated May 17, 2006 has been entered. Claims 37-42 have been cancelled. No new claims were added. Claims 35, 57, and 64-67, have been amended.Claims 35, 36 and 43-67 are pending in the application. Claims 35, 36, and 47-67 are currently under examination.

Response to Objections to the Specification/Abstract

The abstract of the disclosure was objected to in the previous office action dated May 17, 2006. Applicants have supplied the abstract on a separate sheet, apart from any other text. Hence, the previous objection is withdrawn and the new abstract entered.

Response and New Claim Objections – Duplicate Claims

The following new grounds for rejection are necessitated in part by Applicants' amendment of the claims.

Claim 58 was objected to under 37 CFR 1.75 as being a substantial duplicate of claim 57, in the previous office action dated May 17, 2006. In view of Applicants' amendment of claim 35, introducing new limitations that are now encompassed by claim 58, the previous objection is hereby withdrawn.

Claims 43-46 are newly objected to as depending from canceled claims 38 and 39. Appropriate correction is required.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following new grounds for rejection are necessitated in part by Applicants' amendment of the claims.

Claims 43-46 and 53-56 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 43-46 depend from canceled claims 38 and 39. As such, the metes and bounds of their claimed subject matter cannot be determined. It is suggested that the claims be amended to depend from base claim 35.

Claims 53 and 54 are unclear. Claims 53 and 54 recite "a chimeric genetic construct or a vector of claim 35". As a chimeric genetic construct may comprise any sequence, including non-vector sequences, and the vector of claim 35 comprises at least two distinct posttranscriptional regulatory elements, it is not clear to which of the limitations the claims are directed.

Response and New Claim Rejections - 35 USC § 112, Written Description

The following new grounds for rejection are necessitated in part by Applicants' amendment of the claims.

Claims 35, 38-39, 43-46, and 64-67 stand rejected under 35 U.S.C.§112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on pp. 3-5 of the previous office action dated May 17, 2006 is maintained for claims 35, 38-39, 43-46, and 64-67, and further applied to claims 36, 47-56, and 58, due to the amendment of claim 35 to recite "a portion of a UTR region...or a functional portion thereof", and for reasons of record. The cancellation of claims 38-39 obviates their rejections.

Applicants state that the rejection is obviated by the amendment of the claims. Applicants arguments have been fully considered, but not found persuasive. As was indicted in the previous office action, the claims encompass numerous polynucleotide sequences comprising portions or fragments of numerous posttranscriptional regulatory elements that retain functional activity. The recitation of posttranscriptional regulatory elements comprising a functional portion of a UTR does not provide an adequate written description for said functional portion because the specification provides no examples of functional portions or functional fragments of the disclosed sequences which demonstrate that such fragments of promoter or regulatory sequences would actually retain promoter function.

Therefore, the rejection of claims 35, 38-39, 43-46, and 64-67, is maintained for reasons of record and the foregoing discussion, and further applied to claims 36, 47-56, and 58.

Response and New Claim Rejections - 35 USC § 112-Scope of Enablement

The following new grounds for rejection are necessitated in part by Applicants' amendment of the claims.

Claims 35, 38-39, 43-46, 54-56 and 64-67 stand rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide an enablement for the full scope of the invention. The rejection set forth on pp. 3-11 of the previous office action dated May 17, 2006 is maintained for claims 35, 38-39, 43-46, 54-56 and 64-67, and further applied to claims 36, 47-53 and 58, due to the amendment of claim 35 to recite "a portion of a UTR region...or a functional portion thereof", and for reasons of record. The cancellation of claims 38-39 obviates their rejections.

Applicants state that the rejection is obviated by the amendment of the claims. Applicants arguments have been fully considered, but not found persuasive. As was indicted in the previous office action, the specification is not enabling for the broad family of vectors (that include a plasmid, a recombinant virus, a cosmid, an artificial chromosome, an episome etc.) comprising portions of posttranscriptional regulatory elements as gene therapy compositions for treating human disease that include retinal degenerative disease, or methods comprising expressing a transgene encoded by said vectors in fibroblasts and neuronal cells *in vivo*.

Therefore, it is maintained that the specification, is only enabling for a vector comprising a transgene operably linked to at least two distinct posttranscriptional regulatory elements comprising UTR regions selected from WPRE, APP, tau and TH elements suitable for transgene delivery to mammalian cells, and methods for expressing a transgene in mammalian cells *in vitro*, using said vector.

Therefore, the rejection of claims 35, 38-39, 43-46, 54-56 and 64-67, is maintained for reasons of record and the foregoing discussion, and further applied to claims 36, 47-53, and 58.

Response to Claim Rejections - 35 USC § 102

Claims 35-36, 47-51, 53-55, 57-58, and 60-63 were previously rejected under 35 USC § 102(a) as anticipated by Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in the previous office action dated May 17, 2006.

Applicants have traversed the rejection and state that Barry does not describe a vector according to the presently claimed invention. Applicants' arguments have been fully considered and found persuasive. In view of Applicants' amendment of claim 35 to include the limitations of at least one posttranscriptional regulatory element comprising all or a portion of a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR, the previous rejection over the prior art is hereby withdrawn.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

To the extent that claims 53-56 encompass a recombinant cell comprising any chimeric genetic construct and a composition comprising any chimeric genetic construct for treating a human neurodegenerative disease, the following rejection over the prior art is applicable.

Claims 53-56 are newly rejected under 35 USC § 102(e) as being anticipated by Barsov et al. (U.S. Patent Publication No.: 2002/0110896; filed Sep. 24, 2001).Barsov et al. teach recombinant ASLV-derived replication defective retrovirus vectors that can infect mammalian cells for use in gene therapy (Abstract). They further teach that the vectors have an expanded host range and contain a chimeric envelope sequence (claim 6), thus constituting a chimeric genetic construct. The vectors are described as suitable for gene therapy of neurological diseases, such as Alzheimers (paragraph [0081], p. 7) and may be administered in a pharmaceutically

acceptable carrier (paragraph [0090], p. 8). The transfection of cells for the preparation of virus particles is described in paragraph [0106], p. 9.

Therefore by teaching all the limitations of claims 53-56, Barsov et al. anticipate the instant invention as claimed.

Response and New Claim Rejections - 35 USC § 103

The following new grounds for rejection are necessitated in part by Applicants' amendment of the claims.

Claims 35, 37-38 and 46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al. (J. Biol. Chem. 274:2532-2538; of record). Claims 39 and 43 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al. (J. Biol. Chem. 274:2532-2538; of record), and further in view of Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record). Claims 40, 44, and 64-65 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al. (J. Biol. Chem. 274:2532-2538; of record) and Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record), and further in view of Rogers et al. (J. Biol. Chem. 274:6421-6431; 1999; of record). Claims 41-42, 45 and 66-67 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view Paulding et al. (J. Biol. Chem. 274:2532-2538; of record) and Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record), and Rogers et al. (J. Biol. Chem. 274:6421-6431; 1999; of record), and further in view of Aronov et al. (J. Mol. Nerurosci., 12:131-145; 1999; of record). Claims 52, 56 and 59 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Chang et al. (Curr. Gene Ther. 2:237-251; 2001).

The rejection set forth on pp. 13-19 of the previous office action dated May 17, 2006 is maintained for claims 35, 37-46, 52, 56, 59, and 64-67 and further applied to claims 36, 47-51, 53-55, 57-58 and 60-63 for reasons of record. The cancellation of claims 37-42 obviates their rejections.

Applicants have traversed the rejection and state that Barry does not describe a vector according to the presently claimed invention and that the secondary references fail to cure these deficiencies. Applicants further argue that none of cited documents, individually or in combination, describe or suggest a vector according to the claimed invention, suitable for transgene delivery into mammalian cells, containing a chimeric genetic construct containing a transgene operably linked to at least two distinct post transcriptional regulatory elements functional in mammalian cells, at least one of the posttranscriptional regulatory elements comprising all or a portion of a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR or a functional portion thereof. Applicants' arguments have been fully considered, but not found persuasive.

As was indicated in the previous office action of May 17, 2006, Barry et al. describe the generation of lentivirus vectors by combining several posttranscriptional regulatory elements that synergistically increase transgene expression. Barry et al. teach lentiviral vectors for provirus integration into nondividing mammalian cells, wherein the incorporation of two distinct posttranscriptional regulatory elements, namely a central polypurine tract (cPPT) and a human hepatitis virus posttranscriptional regulatory element (PRE) that provide increased transgene expression. The cPPT acts to increase nuclear transport of the virus preintegration complex and thus increases transduction efficiency (first column, p. 1104). As the instant specification does not define or limit the structure of a posttranscriptional regulatory element, the cPPT qualifies as a posttranscriptional regulatory element. Additionally, the lentiviral vectors of Barry et al. encode both GFP and EPO (second column, p. 1104), and are therefore a chimeric genetic construct. Hence, Barry et al. describe a lentiviral vector comprising two distinct posttranscriptional regulatory elements functional in mammalian cells, and further provide the motivation to include two distinct posttranscriptional regulatory sequences, or to substitute or combine additional posttranscriptional regulatory elements with their vector, to increase transduction and stabilize virus vector mRNA for increased transgene expression (first column, p. 1104). The different UTR elements are described in the secondary references, where their presence in the vector leads to increased transgene expression. As Barry et al. describe the synergistic effects obtained by combining two distinct posttranascriptional regulatory elements, it would have been obvious for a person of ordinary skill in the art to substitute any of the known

UTR elements for the posttranscriptional regulatory element of Barry et al. (PRE) with a reasonable expectation of success.

Therefore, the rejection of claims 35, 37-46, 52, 56, 59 and 64-67 is maintained for reasons of record and the foregoing discussion and further applied to claims 36, 47-51, 53-55, 57-58 and 60-63.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(703) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER